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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DANG, IAN D	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/803,459	GERTLER ET AL.	
	Examiner	Art Unit	
	Ian Dang	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *1-5 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II, claims 6-20 in the communication filed on 09/14/2005 is acknowledged. The traversal is on the ground that there is no undue burden to search Groups I and II. This is not found persuasive for the following reasons:

Applicant's attention is directed to MPEP 808.02 which states that "Where the related inventions as claimed are shown to be distinct under the criteria of MPEP 806.05(c-I), the examiner, in order to establish reasons for insisting upon restriction, must show by appropriate explanation one of the following: (A) Separate classification thereof: (B) A separate status in the art when they are classifiable together; (C) A different field of search." As set forth in the Restriction requirement, the separate classification established for each Group demonstrates that each distinct Group has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search. Thus, the Restriction requirement is proper.

Applicant argues that no burden is placed on the examiner to consider all claims. As discussed above, the separate classification established for each Group demonstrates that each distinct Group requires a separate field of search, and a search of one Group would not reveal art on the other Groups, thus imposing a burden on the examiner. Furthermore, each group requires a non-coextensive sequence and non-patent literature search.

The requirement is still deemed proper and is therefore made FINAL. Claims 1-5 and 21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b).

Claims 6-20 are pending and under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting a level of free leptin and a kit for an assay of a level of free leptin in a sample from a human and ovine comprising contacting a sample with a chicken leptin receptor domain, does not reasonably provide enablement for a method for detecting a level of free leptin and a kit for an assay of a level of free leptin in a sample from any individuals comprising an avian leptin receptor binding domain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include: (1) Nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the breath of the claims, (7) the quantity of experimentation needed, (8) relative skill of those in the art.

Nature of the invention and breath of the claims

The claims are drawn to a method for detecting a level of free leptin and a kit for an assay of a level of free leptin in a sample from an individual comprising contacting the sample with an avian leptin receptor binding domain for a time sufficient to allow binding between the free leptin and the leptin receptor binding domain. The invention is broad because the recitation of claims 6 and 14 encompasses any avian leptin binding domains including quails, turkey, pigeons, geese, with any samples, including plasma, serum, blood of any mammals. Although

the chicken leptin receptor binding domain binds to the free leptin in the serum of human or sheep, other avian leptin receptor binding domain may not have different binding requrirements from the chicken one. In addition, the recitation is drawn to a condition or disorder related to level for free leptin.

Unpredictability and state of the art

Horev et al teach that while the leptin receptor genes have been well characterized in mammalian species including human rat, pig, sheep and cow, the leptin receptor genes in other species are not well characterized (page 96, column 2, 2nd paragraph). Horev et al. disclose the first molecular cloning of the chicken leptin receptor gene representing the first characterization of a non-mammalian leptin receptor gene (page 101, column 2, 2nd paragraph). Since leptin receptor binding domain of other avian species have not been characterized at this time, it is possible that these binding domains may be not be able to bind to free leptin because they lack homology to the chicken binding domain. The art is silent regarding the characteristics of non-mammalian leptin receptor genes except for chicken.

In addition, Horev et al. teach that sequence similarities between the chicken leptin receptor gene and corresponding mammalian genes comprises 59-62% identical nucleotides and 49-51% identical amino acids (page 103, column 2). Despite these low homology percentage between chicken leptin receptor gene and that of mammalian leptin receptor gene, the binding occur through the conservation of a few amino acids in the leptin binding domain of the receptor. In other avian species, these amino acids may not be conserved. In view of these teachings, while chicken receptor binding domain binds to human and ovine free leptin, other avian may not be able to bind to human free leptin.

The amount of direction or guidance present

Applicants' disclosure is limited to the use chicken leptin receptor binding domain with free leptin from human or ovine serum. The specification does not provide guidance or direction whether chicken leptin binding domain is able to bind to free leptin from serum of rat, mouse, porcine, or bovine. In addition, the specification does not provide guidance or direction as to what is encompassed by a condition or a disease related to the level of free leptin in the sample. Although Applicants have disclosed that a method for measuring free leptin, Applicants have not provided guidance whether an increase or decrease in free leptin levels correlate with abnormal leptin metabolism and is indicative of a pathological disorder. Since Applicants have not linked free leptin levels with any disorders, modulations of free may not be indicative of any disorders.

Working Examples

Although Applicants have provided examples for detecting free leptin in human and ovine serum with chicken leptin binding domain, the specification does not provide any examples regarding a method for detecting free leptin in mammals with any other avian leptin receptor binding domains. In addition, Applicants have not disclosed any examples measuring abnormal free leptin levels in serum samples associated with a disorder or pathological condition related to leptin metabolism.

The quantity of experimentation needed

Because the claims are broadly drawn to a method for detecting a level of free leptin and a kit for an assay of a level of free leptin in a sample from an individual comprising contacting the sample with an avian leptin receptor binding domain for a time sufficient to allow binding between the free leptin and the leptin receptor binding domain and because Applicant's disclosure does not contain sufficient teachings to overcome the unpredictability taught in the

art, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kratzch et al. (2002) in view of Horev et al. (2000).

The claimed invention is drawn to a method for detecting a level of free leptin and in a human serum or plasma sample from an individual comprising contacting the sample with an avian leptin receptor binding domain for a time sufficient to allow binding between the free leptin and the leptin receptor binding domain to form a bound complex, wherein the receptor binding domain is bound to a solid phase including a micro-titre well plate. The antibody label is radiolabeled, chemiluminescent, electroluminescent, fluorescent, enzyme-labeled, or bioluminescent. The avian leptin receptor binding domain for this assay is derived from the chicken leptin receptor binding domain and the sample is derived from a mammal, which includes a human, rat, mouse, ovine, porcine, or bovine. In addition, the claimed invention is further drawn to a kit for an assay of a level of free leptin levels in a sample from an individual comprising an avian leptin receptor binding domain bound to a solid phase, an antibody having binding specificity for leptin, and a detectable label coupled with the antibody, wherein the free

leptin in the sample binds to the avian leptin receptor binding domain and the antibody binds to the free leptin thus allowing specific detection of the free leptin in the sample.

Kratzsch et al. teach a method and kit for detecting free leptin levels from human serum samples with the human binding domain of leptin soluble receptor. Kratzsch et al. teach a method to capture free human leptin based upon its ability to bind to the soluble extracellular domain of the human leptin receptor forming a complex. Human recombinant leptin receptor binding domains were attached to a microtiter plate and human serum samples were assayed for free leptin. Subsequently, the enzyme-linked antibody, anti-rabbit IgG-peroxidase conjugate, was added to the plate for detection of free leptin (page 128, column 2, 2nd paragraph). Abnormal leptin levels are associated with obesity but also other metabolic diseases such as diabetes (page 128, column 1, 2nd paragraph). Kratzch et al. do not teach the use of the avian leptin receptor binding domain.

Horev et al disclose the average sequence similarity between the CLEPR gene and the corresponding genes comprises 59-62% identical nucleotides, 49-51% identical amino acids plus conservatively changed amino acids. However, there is a much higher sequence similarity among the mammalian leptin receptor genes: 80-92% identical nucleotides, 74-91% identical amino acids, and 90-96% identical plus conservatively changed amino acids (column 2, page 103). While the sequence similarities of amino acid similarity between the chicken and mammalian leptin receptor genes are low, several regions are conserved and strongly suggest functional conservation. One example is the Trp-Ser-X-Trp-Ser motif implicated in ligand binding and signal transduction of cytokine receptor gene family. This motif is conserved between the mammalian and chicken leptin receptor genes. In the chicken leptin receptor, the Trp-Ser-X-Trp-Ser motifs are precisely conserved in terms of sequence and positions of the extracellular region located in the ligand binding domain of the receptor (page 104, column 1).

It would have been prima facie obvious for one of ordinary skill in the art at the time of the invention was made to use the chicken ligand binding domain of the leptin receptor as taught by Horev et al. for a method for detecting a level of free leptin and a kit for an assay of a level of free leptin in a sample from an individual. One of ordinary skill in the art at the time the invention was made would have been motivated to do so because it would reduce the cost and increasing efficiency for manufacturing a kit for an assay of a level of free leptin in samples from numerous different species. Accordingly, the invention taken as a whole is *prima facie* obvious.

Conclusion

No claims are allowed

Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ian Dang whose telephone number is (571) 272-5014. The examiner can normally be reached on Monday-Friday from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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October 10, 2006

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